

*Experimental observations on the pathology of lupus, with notes on three cases of lupus or tuberculosis of the skin of the hand.*

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[With Plate XVIII, figs. 3 and 4.]

THE pathology of lupus has in recent years attracted much attention, and the advances made are familiar to most of us. The opinions of Continental authorities on the subject were fully exposed in the discussion which took place at the International Medical Congress in Copenhagen in 1884, when M. Leloir communicated a paper on the subject, in which he contended that lupus was a local form of tuberculosis of the skin. This proposition was combated by Kaposi and others. More recently Schwimmer, in a paper read before the German Congress of Surgeons, has followed the same line of argument as Kaposi. The latest contribution to the subject, by our greatest authority, Mr. Hutchinson (Harveian Lectures, 1887), is little more favorable to the tubercular theory of lupus. Mr. Hutchinson apparently considers the disease as a non-specific inflammation having locally infective characters. He says in effect that whilst some of the subjects of the disease have the strumous or tubercular constitution, a large number enjoy otherwise sound health.

Most of the arguments adduced on either side may be briefly stated as follows:

The view that lupus is a local tuberculosis of the skin is sup-

ported by these considerations: First, the identity of the histological structure of lupus and tubercle. Essentially lupus consists of granulation tissue; and, as Friedlander has demonstrated, giant-cells are sometimes present. Secondly, the existence of Koch's tubercle bacilli in lupus. Koch has stated that he cultivated lupus bacilli for sixteen generations without observing any difference between them and tubercle bacilli. Thirdly, positive results of inoculation experiments on animals. Guinea-pigs inoculated beneath the skin or in the peritoneum with lupus become affected with general tuberculosis. Fourthly, it is stated that transition forms exist between the varieties of lupus and of tuberculosis of the skin. Fifthly, tubercular manifestations are sometimes coincident with lupus, and it has been estimated that in ten cases of lupus one becomes affected with phthisis. Sixthly, that the disease has a tendency to spread, is locally contagious, and frequently recurs after destruction.

In answer to these assertions it has been urged by Kaposi, Schwimmer, and others: First, that giant-cells are found in simple inflammations, and are not characteristic of tubercle. Secondly, that the bacilli are exceedingly scanty in lupus, whereas they are very abundant in tuberculosis of the skin, and that other well-known pathogenic bacilli possess the same staining reaction, among them being the smegma bacillus of Alvarez and Tavel. But I may add that the smegma bacillus only possesses this reaction when grown in its natural habitat and surrounded by fat. Thirdly, that tuberculosis affects primarily the mucous membrane, and is usually a secondary manifestation in the skin, the reverse holding good in the case of lupus. Fourthly, lupus in man is rarely followed by general tuberculosis or affection of the internal organs. Fifthly, the different effect of treatment of the two diseases, lupus being often cured by scraping and caustics, whereas tuberculosis is not favorably influenced.

Schwimmer also remarks that while general tuberculosis has been developed by the inoculation of lupus in guinea-pigs, a local disease resembling lupus has never been produced. It has been stated by Leloir and others that rabbits are not affected by lupus, while they take tuberculosis readily, and I have shown that visceral tuberculosis may be communicated to rabbits by inoculation of the local form of tuberculosis known as strumous gland disease.

Although, as may be seen, much has been done to elucidate the pathology of this malady, some links in the chain still remain incomplete. I have brought forward the subject this evening with the view of showing that true lupus, as a local disease, may be produced artificially in animals.

On May 7th, 1886, I obtained the following positive results:—A large rabbit was inoculated beneath the skin of the ear with tissue from an undoubted case of lupus vulgaris of the nose, in which there was a good deal of papillary overgrowth. On May 20th the seat of inoculation was marked by a scab, beneath which was some caseous pus. Subsequently a large ulcer covered by a thick scab formed, and soon after an ulcer possessing precisely similar characters broke out at the root of the ear at the distance of one inch from the spot first inoculated. The ear was much swollen, oedematous, hot, and all the hair was lost. In time the scab separated, and healing took place, leaving thickened nodules beneath the skin on the surface of the ear corresponding to the position of the ulcers. The animal was killed on December 16th, 1886, and no trace of visceral tuberculosis could be detected. The lymphatic glands of the neck on the same side as the ear inoculated were healthy. (The ear was exhibited.) I did not obtain the next positive result with primary inoculation of lupus tissue until some time afterwards, and therefore remained doubtful whether that obtained in the first case was not accidental. On November 28th, 1887, I inoculated a large strong rabbit in the same manner in the ear. On December 3rd the ear was much swollen and oedematous. On the 8th the following note was made:—“The ear is still much swollen. At the seat of inoculation is a dry patch, over which the skin is superficially destroyed. Above this, but not continuous with it, is a round dryish ulcer, and on one side of this, again, is a blister of considerable size. The left ear was inoculated from one of the ulcers on the right.”

13th.—The larger ulcer at the seat of inoculation has extended downwards, and is of a dry character. The smaller ulcer above is covered with a dry scab. A superficial ulcerating process, without distinct necrosis, has also appeared on the posterior margin of the ear, which has led to slight destruction. I removed the scabs, and Mr. Lewin made the accompanying drawing (Plate XVIII, fig. 4), which faithfully represents the condition then observed. Near the base of the ear is a long oval ulcer with a

dryish, dusky-red surface, and somewhat undermined margins, to which a few scabs are adherent. This was the site of the inoculation. Some distance above and entirely disconnected with it, is a smaller ulcer having the same characters. It may be seen that the posterior margin of the ear is superficially eroded. On the left ear is a rounded nodule filled with caseous pus produced by inoculation with a scraping from the ulcer on the right ear. On the 30th the ulcerations on the right ear were cicatrised, leaving very considerable thickening (the ear was exhibited). On January 5th, 1888, no ulcer had formed at the site of inoculation on the left ear, but a superficial ulceration precisely like that observed on the right had commenced on its posterior margin. Between it and the caseous abscess were white nodules and white ramifying thickenings or cords apparently marking an extension of disease along the lymphatics of the ear. They reminded one of the tuberculous lymphangitis observed by Leloir in connection with a case of lupus of the left hand (see 'Annal. de Dermat. et Syph.', 1886, vol. vii).

It can hardly be denied that the disease produced in the ears of these two rabbits was true lupus. The inoculation was followed by spreading ulceration covered by a dry scab. The disease was not only locally contagious but the contagion was transmitted to more or less distant parts, for in each case ulcers formed apart from the site of primary inoculation. A considerable destruction of skin took place and a depressed scar resulted. In the second case nodules and cords were observed in the neighbourhood of the ulcer, which might perhaps be considered analogous to the gelatinous deposits around lupus of the face in the human subject. On December 7th, 1887, a young rabbit was similarly inoculated. On the 13th the skin at the site of inoculation appeared to be dried up, and there was a corresponding swelling on the inner side of the ear. Subsequently a dry ulcer formed which began to heal on the 30th, and cicatrisation was completed on January 10th, 1888.

I also inoculated two rabbits with the organs of a guinea-pig to which tuberculosis had been communicated by placing pieces of lupus in the abdominal cavity. There were miliary nodules in the liver. The spleen was much enlarged and filled with nodules of caseous matter, and both testicles were affected with well-marked tuberculosis. One rabbit, inoculated in the ear, developed a perfectly dry, superficial ulcer, which extended with an undermined margin.

No suppuration or scabbing took place, and the rest of the ear remained unaffected.

The other rabbit was inoculated in the anterior chamber of the eye and in the ear. A caseous nodule formed on the ear, but no ulceration occurred. The mass in the eye did not grow, and produced no inflammation. This animal was killed after the lapse of six months, and was found to be perfectly free from visceral tuberculosis; the other is still living. It would therefore appear as if the virulence of the disease was not increased by passing it through the guinea-pig, as is the case with most local tuberculoses, and the results obtained resembled rather those sometimes following inoculation of strumous glands beneath the skin of the ear of rabbits rather than those of my previous experiments with lupus. Briefly to sum up the results of these experiments it may fairly be contended that lupus, as such, has been produced in rabbits, and the missing link in the chain of evidence referred to by Schwimmer has been supplied. This appears of much greater importance as evidence of the close relation of tubercle and lupus than is manifest at first sight.

In the human subject lupus is modified by the age and constitution of the patient, and also according to the vital energy and activity of the circulation in the part affected. But the different degrees of susceptibility of various animals to the tubercular virus enable us to obtain still wider diversities than are usually observed in man. Thus, in guinea-pigs, which possess in the highest degree a tuberculous constitution, we have general tuberculosis almost invariably produced by inoculation with lupus. (In one of my experiments there was also a dry ulceration in the groin which was the seat of inoculation. I readily demonstrated, by means of Neelsen's method, tubercle bacilli in small numbers in the tuberculous lesions of the viscera of this guinea-pig.) In rabbits, which possess in a lesser degree the tuberculous constitution, we have a destructive and locally contagious ulceration without constitutional affection. These facts, together with the knowledge that a certain, although perhaps small, proportion of lupus patients do become affected with phthisis and local tuberculosis, render it difficult to escape from the conclusion that lupus is a modified tuberculosis. The circumstance that by the direct inoculation of lupus in the ear of rabbits in some cases an extensively destructive ulceration was produced, whereas by the

inoculation of lupus passed once through the guinea-pig only a slight superficial ulceration or cold abscess resulted, calls for some comment. It suggests to me that the ulcerative character of some forms of lupus may depend on a mixed infection with perhaps tubercle bacilli and some form of micrococcus favouring suppuration and ulceration.

It has been stated that micrococci are not found in lupus. I was, however, able to stain large masses of micrococci in the specimen of lupus with which the experiment first mentioned was performed. I regret that my present opportunities rendered it impossible for me to follow out the experiments bacteriologically. Since, however, Koch has demonstrated and cultivated bacilli, identical with those of tubercle, in lupus there is little encouragement for other observers to prosecute inquiry in that direction.

I now turn to some clinical aspects of the subject pointing to a close relationship between lupus and tuberculosis of the skin. Doutrelepoint has recently placed on record two cases ('Arch. f. Dermat.,' Heft i, 1888, p. 98) in one of which lupus and tuberculosis of the skin existed in the same individual; in the other, lupus scrofuloderma, and tuberculosis. Within the last month I was much impressed by two patients, both boys, who came under my care. In one angular curvature of the spine, lupus vulgaris of the face and phlyctenular ophthalmia coexisted; the other also had angular curvature and a lupus or tuberculous nodule on the back of his left hand. I excised the nodule. This and the two subjoined examples of tuberculous lesions of the hand seem in many respects to stand midway between lupus and tuberculosis, and may merit a brief description.

*CASE 1. Angular curvature and lupus? on dorsum of hand.*—The nodule formed a distinct, raised, firm, plaque, the size of a half-crown piece. Its edges shelved abruptly. Its surface was dark red, slightly rough, with evident thickening of epithelium, but not ulcerated. It had remained unchanged for some three or four months. The microscope showed merely dense infiltration of the papillary layer and derma with leucocytes (granulation tissue) which extended down only as low as the sudoriparous glands. The cuticle was thickened, and the interpapillary processes of epithelium were prolonged downwards. There were no giant-cells, no reticulum, no caseous degeneration. Several sections were examined for bacilli but none were found.

*CASE 2. Lupus? of palm of hand.*—This interesting specimen was brought by Mr. Bryant to the College of Surgeons. It comprised a nodule which he had removed from the hypothenar eminence of the palm of the right hand of a man aged 26. Four years previously a tumour appeared at this situation, and was excised eighteen months before the present operation. This growth was examined elsewhere, and stated to be a fibroma, and recurrent growth formed, and was believed, from its appearance and the general circumstances of the case, to be a melanotic sarcoma. The skin covering it was of a faint black tint, raised, and on section a firm material was found to occupy the derma and subcutaneous tissue. Microscopic sections exhibited a nearly uniform mass of reticulated tissue covered by a layer of slightly thickened epithelium. In parts the remains of giant-cells, which had not become completely incorporated with the reticulum, and areas where the reticulum was composed of the broad homogeneous bands so characteristic of tubercle, were observed. But for the most part it was indistinctly fibrillar, forming close meshes, enclosing small nuclei (reticular tubercle).

*CASE 3. Papillary tuberculous formation on dorsum of hand.*—This specimen was presented to the College Museum in 1875 by the late Mr. Gay. At that time it was examined by one of my predecessors, and on account of the overgrowth of epithelium the disease was thought to be epithelioma. I subsequently described it in the catalogue (No. 4078) as follows:—"A hand, on the back of which a patch of skin near the bases of the second and third fingers is thickened and covered with scaly crusts and papillæ. There is no thickening around the patch, but the skin was livid in the recent state. The third finger is represented by a stump, and at its extremity are several separate masses of low papillæ." No history is obtainable; but amputation of the ring finger was probably performed for the same disease as that on the back of the hand. Section of the growth, recently made, showed under the microscope many tubercular areas, containing one or several giant-cells (see Plate XVIII, fig. 3). These occupied the papillary layer and corium. The cuticle was much thickened, forming several layers of cornified epithelium. The interpapillary processes of epithelium were extensively prolonged downwards. The rete Malpighii was infiltrated with groups of leucocytes; and at one point a giant-cell, surrounded by its zone of leucocytes, was completely enclosed

in epithelium. Mr. Shattock has described a similar case in the last number of the 'Transactions' (vol. xxxviii, p. 410).

*Remarks.*—The first case may probably be considered as a tuberculosis of the skin secondary to tuberculosis of the spine, although its appearance, course, and microscopic characters are suggestive of lupus. The second case agrees in its characters rather with lupus than with tuberculosis of the skin. The third case should perhaps be considered as tuberculosis, although its naked-eye appearances are very like lupus. The same condition has apparently been named by different writers *lupus verrucosus* and *tuberculosis verrucosa cutis*.

March 20th, 1888.



## DESCRIPTION OF PLATE XVIII.

FIG. 3 illustrates Mr. Eve's case of Tuberculosis of the Skin of the Hand. (Page 7.)

The section shows a miliary tubercle containing three giant-cells.  $\times 320$  diam.

FIG. 4.—Drawing of a Rabbit's Head after Inoculation with Lupus, exhibited by Mr. Eve. (Page 3.)

Near the base of the right ear is a large dry ulcer, which followed the subcutaneous insertion of fragments from a case of lupus vulgaris. Nearer the tip of the ear is a similar but much smaller ulcer which developed at a distance from the seat of primary inoculation. There is also superficial ulceration of the posterior margin of the ear. On the left ear is a cold abscess the result of inoculation of pus from the ulcer on the right ear.



Fig. 3.



Fig. 4.

